

Effective Environmental Control Methods: What Works and What Doesn't

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In 1929 Storm Van Leuven published his results on treatment of asthma using a “climate chamber.” His design of a room included maintaining low dust levels and a supply of clean air. This experiment was based on the observation that many asthmatics improved when they spent time in the high altitude clinics in Switzerland (1). It was also well known .50 years ago that patients with asthma improved when they were admitted to hospital. Indeed Rackemann included failure to improve in hospital as one of the characteristics of intrinsic asthma (2). Skin testing with house dust extracts was routine in allergy clinics as early as 1935. However, advice on avoidance of house dust was hampered because the nature of the house dust “atopen” was not known. In 1962, Spielsma saw live mites in house dust and she and her colleagues rapidly developed clear evidence that mites were a major source of allergens in dust (3). Research relevant to allergen avoidance as a treatment for asthma can now be separated into four areas of interest:

- i) Biology of dust mites, cockroaches and other living organisms that contribute to the allergen content of houses.
- ii) Immunochemistry of indoor allergens and the development of assays for allergens in dust.
- iii) Analysis of the reasons why patients with asthma improve when they are moved to sanatoria or hospital rooms.
- iv) Detailed studies on techniques for controlling allergens in inhabited houses.

(i) Biology of the Indoor Arthropods: Mites and Cockroaches

Some aspects of mite biology are now well known; i.e. that they live best in warm humid conditions, that they require a “nest” to protect against short term fluctuations in humidity, and that they are photophobic. In addition, it is clear that they can eat human skin scales or fungi but will also thrive on many different complex food sources. The aspects of mite biology that are much less well understood include controlling population size and dispersal within houses (4). Although it is clear from cultures that breeding can be accelerated by optimizing conditions it is not clear how that translates into growth characteristics within a house. Thus, there are still major differences in individual houses which are not explained. Furthermore although it is known that different species of mites will compete in cultures, the relevance of this to mite growth in houses is not clear.

Among the many different insects that inhabit houses, cockroaches are best recognized as a source of allergens. Cockroaches are tropical in origin and thrive in houses that are continuously warm. Thus, cockroach infestation was extremely rare in England prior to the introduction of central heating. In addition, cockroaches require food sources and thrive in houses where food or garbage remains open. However, unlike mites, cockroaches are not dependent on ambient humidity and show great talent in finding water sources within a building. Cockroaches can flourish in overheated multistory buildings in New York or Chicago during winters that are very dry. These insects also flourish throughout the South in any house where food is available and the building is not regularly treated. The sources of allergen from cockroaches are not well defined; cockroaches produce fecal particles which look like ground pepper but these are probably too large to become airborne. They also “lick” trails around a house and thus saliva may also be an important source of allergens. Although it is certain that the number of cockroaches in houses can reach very large numbers, no methods currently exist for accurate measurement and the relationship between roach numbers and allergen levels either in floor dust or airborne is not well established.

(ii) Immunochemistry

The purification, characterization and molecular biology of indoor allergens is now as advanced as it is for pollens. In particular, the allergens of dust mites, cats and the German cockroach are very well defined (5-8). Not surprisingly, these organisms produce many different proteins (some of which are enzymes) and allergic individuals can produce IgE antibodies to a large number of these allergens. The use of a single protein to measure sensitization will underestimate the number of allergic individuals. On the other hand, measurement of a single allergen in house dust may be an adequate index of exposure. Clearly, this depends on several assumptions:

- 1) That the protein or major allergen measured is always produced by the organism. This may not be true if the protein is an inducible enzyme only expressed under certain circumstances, or if there is a closely related organism in which the relevant protein is antigenically distinct.
- 2) That the proteins produced by different sources become airborne in the same form. It is clear that cat allergens remain airborne (unlike mite or cockroach allergens). However, it is assumed that all allergens derived from cats behave in the same way. For the dust mite allergens there is considerable evidence that the Group 2 allergen (Der p 2 and Der f 2) are airborne on different particles to the Group 1 proteins (9). However, the overall behavior of allergens of the two groups is very similar. Preliminary evidence from two groups suggests that cockroach allergens become airborne during domestic disturbance but are not measurable in undisturbed rooms (10,11). Thus, cockroach allergens appear to have similar airborne characteristics to mite allergens, which is in keeping with the fact that most cockroach allergic patients are *not* aware of a rapid onset of symptoms in an infested house.

(iii) Effects of Moving Allergic Patients Out of Their Houses

Although families in the United States move repeatedly they generally take their furniture with them and maintain the “new” house in the same condition as the old. On the other hand, real change may occur when families move from a wet climate to a dry climate. There are many apocryphal stories of patients with asthma improving when they move, but no controlled trials. On the other hand there have been extensive studies on children who are moved from their houses to sanatoria. The most important conclusion is that children kept in these allergen free conditions have decreased bronchial reactivity as well as decreased symptoms of asthma. Results of that kind have been reported from three high altitude sanatoria in Davos, Briancon and Misurina. Similar results have also been shown with young adults admitted to a hospital “allergen free” unit (12,13,14,15).

Dr. Boner and his colleagues in Verona have reported detailed studies on the immunological events that occur during periods of time at a sanatorium (14,16,17). They demonstrated decreases in serum and nasal antibodies, but more significantly they found decreased numbers of eosinophils in induced sputum. It was suggested that decreased numbers of eosinophils in sputum correlated with decreased non-specific bronchial reactivity. The effects of moving to the sanatorium reversed when children went home and studies demonstrated that these effects were reproducible (14-18). These findings strongly support the view that symptoms and bronchial hyperreactivity (BHR) in children with asthma are maintained by continued exposure to antigens in the home. However, it is very important to recognize what the sanatoria and hospital units represent. In addition to having very low levels of mite allergens these units have no carpets, no animals, very low mold spores, good ventilation and in many cases an exercise program. Thus, although the dominant skin sensitivity of the children in each of these studies was to dust mites, it would be simplistic to

assume that the results of moving the children were simply due to mite free conditions.

On the other hand the results of these experiments are the strongest evidence that changing the environment of children can lead to decreased symptoms and BHR. When the results were first reported in 1970 there was very little understanding that asthma was an inflammatory disease. Thus, the avoidance experiments in sanatoria have been a major part of the evidence that i) conditions in houses are a *cause* of asthma and ii) that avoidance measures can be an important form of treatment.

(iv) Detailed Studies on the Techniques Used for Controlling Allergens

If only our patients had the will and the means, avoidance is easy! Thus, an air conditioned (i.e. low humidity) apartment with polished wooden floors, leather or wooden furniture, no animals, and a simple bedroom with covered mattress and pillows is easy to maintain. Indeed, it is not difficult to maintain an “allergen free” hospital provided helpful friends do not bring in stuffed toys and animals such as guinea pigs, rabbits, etc. The major problem is overcoming lifestyles that the family seems unwilling or unable to change. The biggest practical problems can be divided into two groups: (a) carpets, sofas and bedding; (b) and animals.

Carpets, sofas and bedding

Carpets and sofas represent an extraordinarily large reservoir of allergens, humidity and food for dust mites. Traditionally, carpets have been removed regularly and cleaned by beating (England and the USA), laying out in the sun (Finland), or putting out in the snow (Scandinavia). In France, rush matting in Versailles was composted or burned. Inherent in all these procedures is the ability to remove the carpet. Indeed, fitted or wall-to-wall carpets are a modern invention only conceived after the introduction of vacuum cleaners. Beating carpets and/or putting them out in the sun are effective methods of cleaning and killing mites (19). The question then becomes; is it possible to clean and/or kill mites in a carpet that stays on the floor? Studies on vacuum cleaners have focused on the filtering capacity of the cleaner (20). These studies showed that some vacuum cleaners leak more than others and show that double layer bags or additional filters, such as High Efficiency Particulate Air (HEPA) filters, may be highly effective. Recent studies evaluating vacuum cleaners recommended for allergic subjects have confirmed the importance of filtration for minimizing allergen leakage (21). Thus, the major negative effects of a vacuum cleaner can be minimized by good design. On the other hand, it is an illusion to imagine that cleaners can remove human debris from a carpet. All fitted carpets steadily *increase* in weight with time and this is due to accumulated material in the carpet. This debris provides nesting material and food for dust mites, but also makes it exceedingly difficult for acaricides to contact mites in a carpet. Steam cleaning has been recommended; indeed, the companies often claim that this treatment is effective against mites. However, steam cleaning is designed not to reach the bottom layers of a carpet, because these layers are often not colorfast, and water tends to bring up colors as well as old stains.

There are many different chemicals that will kill mites. These include benzyl benzoate, pirimiphos methyl, abamectin, and also some of the complex mixtures marketed as cockroach sprays (22-25). In laboratory experiments benzyl benzoate or pirimiphos methyl will kill mites within a day. Thus, the problem is not *how* to kill mites but how to kill mites where they reside i.e. within a carpet or sofa. With some effective acaricides the problem is compounded because the company is reluctant to market the chemical for domestic use; this has been true for pirimiphos methyl and abamectin. Thus, most acaricides for houses use benzyl benzoate, which has a long record of safe use with humans because it is a preservative for food and a traditional treatment for scabies mites. Benzyl benzoate has been marketed in three forms: as a moist powder

("fucht pulver"); as a foam; and in a liquid together with tannic acid. The foam appears to be ineffective on both mattresses and sofas (25,26). The powder form presents problems related to techniques for application; simply applying the powder and leaving it for a few hours is not effective. If the powder is brushed in, left overnight and brushed in again before vacuuming, it has a significant effect that may last up to 3 months. The liquid forms of benzyl benzoate or benzyl alcohol with tannic acid are not as effective as was originally hoped. This was attributed both to problems applying the fluid and to the chemicals being too dilute (25).

Tannic acid (TA) has been recognized for centuries as an important agent for crosslinking and denaturing proteins. Tannic acid works non-specifically on proteins and it probably requires multiple "bits" with TA to denature a protein molecule. Tannic acid was first studied in detail by Dr. Green in Sydney who demonstrated its efficacy for mite allergens (27). Our group carried out detailed laboratory experiments to test the effects of TA on mite and cat allergens; the results illustrated several problems (28). First, TA was ineffective when applied to high concentrations of cat allergen, and second, the presence of Fel d 1 inhibited the activity of TA against mite allergen in the same mixture. Problems with evaluating TA became apparent in handling dust samples from carpets that had been treated. Dried TA in the dust redissolves resulting in interference with assay measurements and further denaturation of protein in the dust; either of these effects can produce spuriously low allergen measurements. Adding bovine serum albumin (BSA) to house dust extracts caused precipitation of free TA and protected the assay. This is simply a technical problem, but the results illustrate well both the complex nature of interactions between TA and allergens, and potential problems in assessing the effects of chemicals on allergens in carpets. However, results of our studies suggested that TA is more likely to work if the carpet is cleaned first to reduce the total protein content and if it is applied as a 3% rather than 1% solution. Although TA has a reputation for staining, it can be produced in a form that does not stain. On the other hand, applying TA to basement carpets which are damp can bring out old stains creating further problems. In general, TA is an effective denaturing agent that has major effects on mite or cat allergens (29). However, TA has no effect on live mites and the effects are short-lived. Combination with benzyl benzoate is appropriate but the correct mixture has not been established.

Sofas are a special problem both as a reservoir for allergen and as a mite nest. Approaches to mite allergen reduction include controlling humidity (sofas moved to Denver lose their mite population over about a year); freezing with liquid nitrogen (very effective but not practical); and designing a sofa with an impermeable barrier just below the fabric cover; this latter approach may be the best solution in the future. We recently tested the effectiveness of different fabrics in blocking both cat and dust mite allergens. Results showed that fine woven polyester fabrics (pore size 6 μ m) efficiently blocked allergens tested while still allowing up to 40% of the airflow of control fabrics (30). These results suggest that such fabrics could be effective alternatives to semipermeable or impermeable materials as allergen barriers.

Bedding is a primary target for allergen control owing to the high level of mite allergen exposure which may occur while sleeping (31). Studies suggest that encasing bedding (ie. mattresses and pillows) is an effective method for reducing allergen levels (30,32-35). Initially, materials used for encasings were made of vinyl or vapor-permeable fabrics which were uncomfortable. The recent availability of more comfortable, air permeable fabrics which are highly efficient at retaining allergens has made encasing bedding a reasonable approach for all patients in controlling exposure to allergens. It is now feasible to encase pillows with "breathable" fabrics which would prevent dust mite entry into bedding. However, it remains to be tested whether this approach is an efficient method for maintaining "allergen-free" bedding. Encasings should be wiped down each week with a damp cloth to remove any allergen, or washed. Clearly, it is necessary to control allergen levels in blankets and duvets which are not encased. A variety of laundry methods have been shown to be effective at reducing mite and cat allergens in bedding (36-38). As a result of these studies, we recommend that patients wash their bedding in hot water on a weekly basis. It should be

stressed that chemical treatments eg. acaricides, have not proved effective in treating mattresses (39).

Animals

Cats

Domestic animals have been recognized as an important source of allergens in house dust since the early 1920's. Indeed, patients usually give reliable histories of allergic reactions to cats and/or dogs. Despite this, even severely ill patients are often resistant to advice to replace live animals with porcelain ones. If the cat is removed from the house, it will still take weeks for allergen levels to decrease, reflecting the large reservoirs of cat allergen that accumulate in carpets, sofas, etc. (40,41). The major cat allergen, Eel d 1, is primarily produced in the skin and is probably carried on flakes of dander. These "*flakes*" appear to have two very important properties: first, they are sticky and become adherent not only to walls and other surfaces but also to clothing. This facilitates the transfer of cat allergen to other houses which may result in levels of Eel d 1 in houses without a cat comparable to those in houses with a cat, i.e. $\geq 20\mu\text{g}$ Fel d 1/g dust (42,43). Furthermore, it has recently been demonstrated that cat allergen can be airborne in houses without a cat (44). This has very important consequences for avoidance, because most clinics do not consider the possibility that cat allergen is playing a role in symptoms if the patient states that they do not have a cat in the house. Second, particles carrying cat allergen behave aerodynamically as small particles [their actual size is not established but may be larger than their apparent $2\mu\text{m}$ diameter]. These particles or flakes remain airborne for hours and are almost always measurable in the air of undisturbed houses with a cat. Detailed studies on the falling rate of cat allergen after disturbance established that the aerodynamically "large" particles fall rapidly. However, increasing ventilation will remove small particles and tend to keep large particles airborne (45,46). Until recently it was considered pointless to try to control cat allergen exposure in a house with a cat. However, detailed study of Eel d 1 has indicated a range of useful steps and suggested that a radical change in the house could control cat allergen. The obvious measures are:

- Remove reservoirs such as carpets and sofas because very little allergen accumulates on polished floors, leather sofas, or wooden furniture.
- Keep the cat outside as much as possible.
- Use room air cleaners; these can reduce airborne cat allergen if the reservoirs are removed first. HEPA room air cleaners will remove almost all allergen particles from the air that passes through the filter.
- Wash the cat; at present the efficacy of washing cats is disputed. It has been observed repeatedly that sequential washing of cats yields progressively smaller quantities of Fel d 1 (47,48). The first experiments to study airborne allergen coming off a cat after washing also showed very clear results (45). However, subsequent experiments by Kiucka and his colleagues showed only a modest effect one week after washing (49). We have carried out detailed experiments to assess the effects of different washing techniques on cats. The results showed that cats carry a large quantity of allergen (i.e. $\sim 60\text{mg}$) and that even aggressive washing can only remove $\sim 40\text{-}70\%$ of this allergen. The allergen becoming airborne off cats is dramatically reduced 6 hours after washing but decreases do not persist for more than one week (50). These results do not show that cats should not be washed, but suggest that the procedure will not control allergen release for more than a few days. Simple calculation of the allergen coming off a cat suggests that the amount coming off, i.e. $\sim 1\mu\text{g}/\text{hour}$ is $\sim 0.02\%$ of the allergen on the cat. Thus, the factors (e.g. electrostatic charge) controlling whether particles become airborne may be as important as the total quantity of Fel d I on the cat. However, use of a commercially available treatment to wipe on cats was not effective (49,51).

Dogs:

Obvious allergic reactions to dogs are less common than those to cats; however in areas where dogs are kept in houses, they can become an important source of allergens (52). From preliminary results it appears that dog allergen becomes and remains airborne like cat allergen. Thus, it is likely that the same rules apply to dog allergen as to cat. Of course, many dogs are kept outside, which probably reduces the problem. Interestingly, in hotter climates (e.g. Virginia) it is normal practice to wash dogs regularly. A recent study has shown that washing the dog reduces recoverable allergen from dog hair and dander. However, as with cat allergen, reductions in Can f 1 are not maintained for more than a few days (53).

Rodents:

The major source of allergen from rodents is urinary; in particular, the kidneys of male animals *leak* large quantities of protein into the urine. These urinary proteins have been studied, both in terms of the immune response and the form in which they become airborne. Although these experiments were carried out with laboratory animals, they are almost certainly relevant to caged animals at home. The main source of airborne rat allergen appears to be the bedding material. Further, the amount of allergen coming off the bedding is dramatically increased by drying. Particles in wet bedding probably stick together and fall rapidly (54). The first line of treatment for all rodents in the house is eradication. However, controlling exposure to dried bedding is highly relevant to animal allergic laboratory workers, and may be relevant in some houses. Keeping cages out of bedrooms is essential and regular removal of the cage material may also help. Whether saliva is an important source of rodent allergen in the house is not clear, however biting by rats is a remarkably effective method of causing anaphylaxis in rat allergic individuals.

Insects- Cockroaches

The rapid development of immunochemistry of cockroach allergens between 1985 and today has made it possible to measure exposure and begin to study methods of controlling exposure (7,55,56). Talking to patients who are allergic to cockroaches (as judged by skin tests), it is clear that they do not relate their symptoms to exposure to roaches. Furthermore, most of these patients, just like mite allergic patients, do not report rapid onset of symptoms on entering a house which is infested with roaches. In keeping with this, cockroach allergen is not found airborne in undisturbed houses. Thus, the airborne characteristics of cockroach allergens are similar to those of dust mites but not of cats. This suggests that environmental control should focus on reducing the allergen source rather than on air filtration. The highest levels of cockroach allergen have generally been found in kitchens. Although at present we don't have clear data on the effects of eradication measures on cockroach allergen, it is possible to extrapolate from eradication studies. The main approaches include:

- Fastidious cleaning to reduce food supplies, including enclosing all food and disposing of garbage rapidly.
- Closing all entry points with sealants.
- Killing roaches. The best approach is to use bait; traps only catch a small number and the sprays are irritating particularly to allergic individuals. With the best effort controlling cockroaches in some multi-dwelling buildings may be very difficult, but determined effort is usually successful and there is no reason for allowing infestation of a single dwelling unit.

Allergens that are Primarily Outdoors: Fungi and Pollen

We are still in a difficult situation with indoor fungi because the methods proposed for measuring exposure are still very time consuming, i.e. microscopic examination of sticky rods. Furthermore, some of the key species cannot be distinguished by their spores, e.g. *Penicillium* and *Aspergillus*. Cultures are more time consuming and difficult to quantitate. It is clear that mold growth is an important problem in houses and can create a major problem for allergic patients. Surprisingly, the clearest association with asthma is for sensitization to *Alternaria* which is generally regarded as an outdoor mold (57-59). The reason this seems surprising is because many of the *Alternaria* sensitive patients appear to have perennial rather than seasonal asthma implying that exposure is occurring indoors as has been suggested for pollen allergens (60). Taken together, these observations suggest that *Alternaria* may be the most important outdoor allergen today. Recently, an assay has been developed for measuring the *Alternaria* allergen Alt a 1 allowing monitoring of environmental exposure to this allergen (61). Measures for controlling fungal growth are well established and until detailed methods for studying the effects of exposure are developed, these measures should be advised.

Conclusions

Given that allergen avoidance is the primary anti-inflammatory treatment for asthma, it is clear that the treatment should be taken seriously. Furthermore, the ability to measure specific marker allergens in house dust has made it possible to test many of the measures advised to patients. During this process the advice given has become increasingly antigen specific. In general, avoidance can be classified as: (1) source reduction by elimination; (2) source reduction by physical barriers; (3) removing reservoirs; and (4) air filtration. The relative importance of these measures depends on the nature of airborne particles. However, the main reservoirs are very important (i.e. mattresses, pillows, carpets and upholstered furniture) because they act both as a nest for mites (and roaches) as well as a major site in which allergens accumulate. The second major issue is the "air handling"; this is a euphemism since domestic houses don't have controlled air entry, however the issues of humidity, temperature and ventilation rates are almost certainly central to the causes of increased asthma. If we could persuade families to run their houses colder and drier, then mite, cockroach and fungal problems would all decrease. It seems that houses should never be allowed to be hot, humid *and* have large reservoirs for growth of mold and mites. The choice is either to keep the house cool and dry or to remove carpets and sofas, and to cover mattresses and pillows. It is clear that the old model in the South of taking up all carpets in the spring and storing them for the summer was correct.

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